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The Germ Theory of Disease

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with the compliments of the Author.

THE GERM THEORY OF DISEASE.

THE great and ever-growing interest in the question of the relations of vegetable germs to disease has, during the past few years, multiplied the literature of this subject to such an extent that it is difficult, nay, almost impossible, for the general reader to keep himself as well posted as he might desire on this most important subject. For of its importance, who will doubt? It is a question of interest not merely to the physician, but one of the greatest weight to society at large; and it is certainly worthy to rank, along with Cohnheim's discovery of the process of inflammation,—that riddle which had baffled the attempts at solution for thousands of years,—as one of the first medical, or, to put it on a broader basis, biological discoveries of the nineteenth century. We gladly welcome, therefore, two works[1] which, within a moderate compass, give a good synopsis of the present state of our knowledge on this subject.

Though some of the older investigators, as Leeuwenhoeck and Spallanzani, investigated the nature of putrefactive processes, and made discoveries that were forerunners to our present knowledge, yet the real science of mycology, in its relation to disease, dates from the middle of the present century. In 1848 Fuchs discovered micro-organisms in the blood of septicæmic

[1] See under Book Reviews: "Bacteria and the Germ Theory of Disease," by H. Gradle, M.D.; and "On the Relations of Micro-Organisms to Disease," by Wm. T. Belfield, M.D.

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animals; and Brauell and Davaine in 1849 and 1850 observed the anthrax bacillus in the blood of sheep dead of that disease. Still, it was not till 1861, when Pasteur published his work on fermentation, that the relations existing between what are now called bacteria and disease were pointed out. Since then the science of mycology has been making rapid strides. Numerous pathologists in all countries have prosecuted the study, and though, as is perhaps natural, a great quantity of ill-judged work has been hurried into print, and many wrong observations chronicled as facts which, when disproved, have had some tendency to throw the whole subject into contempt with the general medical public, yet, on the whole, the work has gone steadily forward, and this progress we owe principally to two men,—Pasteur and Koch. Pasteur was one of the very first in the field, and labored under the disadvantage of having to invent himself all the methods he used, having but a very small and imperfect stock of the experience gained by others to go by. In spite of these obstacles he has done great and original work, and if all his statements are not marked by the accuracy that distinguishes his German collaborator, and if he is at times given to somewhat bold flights of fancy, due allowance should be made for the national peculiarities of a Frenchman. Koch improved and extended the methods which he found in use, and brought to bear on his investigations a mind too critical, and a judgment too cold, to become warped into partiality by any glittering semblances of truth. His thorough scientific honesty, his truly Darwin-like patience in waiting to thoroughly test by proof and counter-proof the accuracy of his observations, before announcing them to the world in print, his ripe judgment and clear reason, have all borne their fruits, and Koch stands to-day the foremost investigator in this field of science. To him we owe our knowledge of the life-history of the anthrax bacillus,—the work that first brought him into prominence,—and more recently that of the tubercle bacillus.

Bacteria are vegetable cells of various shape, devoid of chlorophyll, and consist of a highly refractive nitrogenous substance,

called by Nencki *mycoprotein.* As they exhibit a high degree of resistance toward the action of acids and alkalies, Cohn has supposed them provided with a covering of some hydrocarbonaceous material like cellulose.

In shape, they may be spherical (micrococci), or rod-shaped (bacilli), or spiral (spirillæ). Many of the rod-shaped varieties have a thread-like appendage at one end, called a flagellum, by means of which they are capable of motion through the liquids in which they reside. The motion so often seen in bacteria when examined in a drop of liquid, as urine, under the microscope, is not necessarily a sign of life, as this motion may be due to the Brownian movement seen whenever small particles are suspended in a liquid. They multiply in two ways, either by a bacterium dividing into two by fission (hence the name *Schizomycetes*, or *Spaltpilze* of the Germans), or by spores forming within them, which are set free by the death and subsequent disintegration of the bacterium.

Bacteria of one kind or another are distributed, as far as we know, everywhere; but some producing very marked and specific changes in the organisms in which they may happen to lodge, as anthrax, malaria, typhoid, yellow-fever germs, etc., etc., are endemic in certain localities, and are plants peculiar to those localities. To cite the best known of these, we will take the *bacillus anthracis*, which causes in animals the disease known as splenic fever; in German, *Milzbrand;* in French, *charbon.* This bacillus occurs in certain marshy districts of Europe, and to a limited extent also in this country, and causes the endemic appearance in the cattle inhabiting these parts of the splenic-fever disease. Koch has discovered that the plant grows as well outside of the body, in a suitable medium, as in it, and this explains the yearly recurrence of the disease at certain seasons of the year in the same localities without fresh infection being introduced from without. He found that the bacillus grows best in an *alkaline* vegetable infusion. Ordinarily, vegetable infusions are acid in reaction, but in these infected localities it has been found

that owing to lime in the soil they are alkaline, and hence afford the desired reaction for the best propagation of the plant.

Cattle, by grazing in these districts, become infected with the spores through abrasions on the lips, tongue, etc.; or, as Koch has also shown, the spores develop in the alkaline fluids of the intestinal canal into the perfect bacilli, which then penetrate the walls, and thus gain entrance to the circulation. Another mode of infection is by direct contagion, one animal coming in contact with the secretions from the mouth or nose, or with the blood, of another already infected. In the living body the bacilli do not go on to sporification, but multiply only by fission; but the bacilli which have been developed in the body from spores, by being eliminated by the secretions, and falling on the earth or grass of the fields in which the cattle graze, form new centres of infection, for here they go on again to the formation of spores. It is doubtful whether direct infection by means of the bacilli is often effected, since these are so easily destroyed. This is in marked contrast to the spores, which may be exposed to great variations of heat and cold, to the action of strong alcohol and other chemicals, without losing their vitality. The bacilli do not develop except at a temperature above 18° C., and in the presence of oxygen.

Pasteur attributed to earthworms the carrying to the surface of the spores developed from the bacilli buried with dead animals, but Koch has shown that at the depth at which animals are ordinarily buried, the temperature in European countries does not usually rise above 18° C., and that the bacilli soon perish. The dropping of the animal secretions containing bacilli is quite enough to account for all sources of repeated infection.

Probably the most widely diffused of all bacteria are those causing putrefaction and fermentation, for they seem to be ubiquitous. They are the great scavengers and chemists of nature, removing useless, dead material, and reconverting it into its original elements, to be used afresh for the making of new bodies, whether animal or vegetable. Different bacteria, morphologically

identical as far as we can determine with the means now at our command, may have very different chemical properties. Thus the *bacillus subtilis* found growing on hay, and the *bacillus anthracis*, are to all appearance exactly alike, yet the one is harmless, while the other is most deadly. Indeed, this very similarity, combined with errors in the experimental methods employed, induced Buchner to believe that the harmless hay bacillus could, by appropriate cultivation, be converted into the fatal anthrax bacillus, and that the two were in reality identical.

Koch, however, exposed the fallacy of this opinion by showing that Buchner's cultures were not pure ones, and that his cultivated hay bacilli had from the very first become contaminated with those of anthrax, which finally had so gained the upper hand as to crowd out the former, and consequently to produce, when inoculated, symptoms due to the latter alone.

Precisely in what way the bacteria induce in the body the changes which they do, is not known, but that they grow at the expense of the food which they consume is evident. Some have been found incapable of living without oxygen, whilst others die in the presence of it, or at least lose their characteristic properties. To the former Pasteur has given the name of *Aërobes*, while to the latter that of *Anaërobes*. That the bacteria by their growth soon exhaust the medium in which they are of its power of nourishing them, is shown by the fact that when in such a medium all further growth has come to a stand-still, by transferring a portion of its bacteria to a fresh culture-ground, their growth will go on uninterruptedly until this medium in its turn becomes exhausted.

In some cases it has been most clearly shown that the disturbances produced in a living body by the presence of organisms in it, are due not directly to their mere mechanical presence, but to the effects of some substance elaborated by them in their growth, and which acts as a poison upon it. Thus Panum induced symptoms of great depression, vomiting, purging, collapse, and finally death, with or without fever in different cases, in dogs in which he

had injected varying quantities of a carefully filtered solution of rotting nitrogenous substances. Possibly these effects were due to the ptomaïnes, those cadaveric alkaloids which, as Selmi has discovered, are produced in decomposing organic remains. Bergmann and Schmiedeberg found in putrid yeast a crystallizable substance which they called *Sepsin.* This when injected produced in dogs immediate fever and the intestinal symptoms of putrid poisoning.

In pyæmia we have a disease characterized by a septic fever, accompanied by the formation in various organs of metastatic abscesses. These abscesses are caused by the deposition in the different organs of emboli containing micrococci, which when once lodged cause a local suppuration by their growth. The micrococcus of pyæmia Koch has found to grow in colonies in the blood-vessels, and to cause thrombi in them, by surrounding the blood corpuscles, and thus rendering them more adhesive. Parts of these thrombi are torn off and are carried into the circulation as emboli, taking with them the micrococci, and causing, as we have seen, those metastatic abscesses characteristic of the disease. If the blood of a pyæmic animal, after having been carefully filtered through clay, or having its bacteria killed by boiling, be injected into another animal, a septicæmia alone will be produced, without the formation of metastatic abscesses; and, furthermore, the blood of the second animal is not infectious, showing that while pyæmia with metastatic abscesses is due to the growth of a living specific bacterium in the organs, septicæmia is caused by the poison elaborated by the bacteria being introduced into the system. This may occur from the absorption of the secretions of a wound alone, the bacteria themselves not gaining an entrance to the body. It may be due also to the presence of various kinds of bacteria, some micrococci, some bacilli, as Koch, Gaffky, Pasteur, and Sternberg have shown.

It would almost seem as though the febrile symptoms of septicæmia were due to the disintegration of the white blood globules by the septic poison, and the setting free thereby of fibrino-plastin

and fibrin-ferment, for the blood of septicæmic animals contains more free fibrin-ferment than normal, and Bergman and von Angerer, as well as others, have found that the injection into the circulation of small quantities of pepsin, trypsin, and other ferments which effect a liberation of fibrin-ferment, cause a fever exactly like that of septicæmia—observations which we have had the opportunity of confirming. Still, we are as far off as ever from the ultimate knowledge of how this fibrin-ferment should cause fever, even if it does, as the authors just mentioned affirm, produce a capillary embolism by coagulation of the blood. Besides, of the existence of this capillary embolism no really satisfactory proof to our mind is brought.

The aseptic fever of Volkmann, noticed after subcutaneous contusions, after simple fractures and the like, is considered to be due to the absorption of the products of the extravasated and disintegrating blood.

It would seem that while pyæmia is produced, as far as we now know, by but one kind of bacterium, septicæmia and suppuration may be due to various kinds.

Ogston and others have constantly found micrococci in the pus of acute abscesses, even in those in which no communication with the air could be discovered. This pus, injected under the skin of guinea-pigs and mice, caused symptoms of blood-poisoning, followed by a local abscess, in which, and in the blood of the affected animals, numerous micrococci were found. No metastatic pyæmic abscesses were found, and the animals usually recovered after the lapse of five to seven days. These micrococci, Ogston observed, were usually grouped together in clusters or in chain-form, and they preserved these arrangements when artificially cultivated. Pasteur found a micrococcus in furuncles, which, when injected under the skin of animals, caused suppuration there, though injected into the blood-vessels it proved harmless.

Some kinds of bacteria may exist in wounds without causing any suppuration, for such have been found by Cheyne, in wounds running an entirely aseptic course, and the writer has frequently

observed in the water-blisters produced on the hands by rowing or other exercises where the skin is chafed, that the fluid contained in them is full of micrococci, although no visible communication exists with the air. Here the micrococci evidently must gain entrance by perforating the epidermis. Every one of us must have had such blisters at one time or another, and yet we all know that they do not go on to suppuration.

A great deal of interest has been shown in the question as to whether putrefactive bacteria may not pre-exist in the blood and tissues of normal animals, and many experiments have been made to settle this point. The result of most of these experiments was to indicate quite strongly that these bacteria really did pre-exist, when the positive experiments of Meissner, as detailed by Rosenbach, in the *Deutsche Zeitschrift f. Chirurgie*, vol. xiii, 1880, threw them all into the shade. Meissner, by filtering the air and water in which he kept the various tissues taken from living animals, was able to preserve the latter entirely undecomposed, and without the aid of any disinfecting chemicals whatever, for an indefinite length of time—up to two years. Such positive experiments are worth any number of negative ones.

It is a universal experience that one attack of an infectious disease, as measles, scarlet-fever, small-pox, etc., gives immunity to subsequent attacks. The reason for this is not clear. The opinion has been advanced, that the bacteria, to which the infectious diseases are due, by their growth in the body remove from it that certain something which forms a suitable soil for their propagation, and that this is not reproduced. In view of the fact that the constituents of the body are so constantly undergoing changes, the old being replaced by the new, this idea seems hardly tenable ; still, as yet no better hypothesis has been offered.

The preventability of infectious diseases is a subject that, from the very beginning of our knowledge of disease germs, has occupied the attention of investigators, and has, in their hands, met with a great deal of success. The methods employed are two. The first seeks to exclude the germs entirely from entering the

system and gaining a foothold there: The second endeavors, by the inoculation of a "mitigated virus," to produce a mild form of what would otherwise be a severe, perhaps fatal, disease; this mild form, however, having the same effect as the severe one, of giving immunity—for some time at least—to subsequent invasions of the germ. In the first category are embraced all quarantine and hygienic regulations generally, as applied to communities; and, to individuals, the Listerian treatment of wounds. In Listerisim—and by that term we do not mean merely an observance of the details of gauze, carbolic acid, macintosh, rubber protective, spray, etc., etc., that go to make up a "Lister dressing," but the application of disinfection to wounds in its widest sense, whether with chemicals or without,—in Listerism, we say, we have a recognition of the fact that the unhealthy suppuration of wounds, and its bad after-effects upon the body, are due to the presence of bacteria in the exposed parts, and the absorption from the latter either of the germs themselves into the body, or the products of their growth, which act as a poison on the tissues. Inoculation of small-pox has been practised in China from the very earliest ages, but it was not till 1717 that Lady Mary Wortley Montagu introduced it into England, where, after much opposition, it became popularized, only to be superseded by vaccination, first employed by Jenner in 1796. The method pursued in inoculation was to take the virus from the pustule of a small-pox patient after the eighth day, and to introduce this beneath the skin of the person to be inoculated. The disease which followed resembled ordinary small-pox, excepting that it was much milder in degree; like it, too, it was characterized by a general eruption. Jenner, already in 1770, communicated to John Hunter his observation, that persons infected with cow-pox from milking affected animals, remained exempt from small-pox, but it was not till 1796 that he actually practised vaccination on a child. The subsequent progress of vaccination is too well known to need further comment.

In the past few years, Pasteur, Toussaint, Chauveau, and others, chiefly of the French school, have given much attention to the

prevention of anthrax, chicken cholera, and some other infectious diseases affecting animals. Their idea has been to render by various ways the bacteria less active in their manifestations than before, while yet retaining enough vigor to grant immunity against attacks of the unchanged plant. Pasteur's mode of "attenuating" the anthrax bacillus is to keep it permanently at a temperature of 42°–43° C. in neutralized chicken-broth. Its vitality is thus gradually lowered, till at about the end of a month it dies. By using the cultivations at different times within this period different degrees of intensity may be reached. Pasteur claims that the bacillus undergoes an actual physiological modification, but whether it does so or not is still a disputed point with mycologists. Some assert that its effects are due simply to dilution, for the same effects have been produced by using for inoculation a highly diluted virus. When we remember that in the body the anthracis bacilli do not go on to the formation of spores, and multiply only by fission, and this to a not unlimited extent, it seems plausible enough to suppose that a few bacilli would produce symptoms less severe than if many were introduced into the system. On the other hand, the decrease in the virulence of epidemics toward their close, indeed, the fact that they cease at all even when there are plenty of unaffected individuals about, would seem to be a point in favor of a physiological change,—a certain decrepitude, so to speak,—gradually overtaking the later generations of the germs. Again, in vaccine and in small-pox, we seem to have another evidence pointing strongly to modification by soil. Cow-pox inoculated on man gives immunity against variola. The contents of a true variolous pustule from a human being, on the other hand, inoculated on a heifer, produce cow-pox, which, however, in turn produces the latter disease again in man.

While the cause, therefore, is yet to be settled, the fact nevertheless remains that the inoculation of cattle has been successfully practised on a large scale in France, Germany, Hungary, Holland, the Cape of Good Hope, etc., both for anthrax, pleuro-pneumonia, and tagsore (variola of sheep). It does not, however,

give perfect immunity in all cases, especially from infection by way of the alimentary canal. Extensive experiments are being carried on at the present time which will, no doubt, throw more light on this question, so highly important from an economic point of view.

In the past year and a half the most important discovery announced in mycology is that of the *bacillus tuberculosis* by Koch, who in a comprehensive series of experiments that have since been widely repeated, demonstrated that the disease tuberculosis is due to the invasion of the body and the growth in it of a bacillus. Koch's discovery was the last link in the chain needed for the absolute proof of the bacterial origin of tubercle, for the experiments of many observers, notably Cohnheim, had shown that it was a truly infectious disease, due most undoubtedly to an organized inoculable virus.

The presence of bacteria of one form or another has been demonstrated in a number of diseases besides those already mentioned, as erysipelas, gonorrhœa, syphilis, lepra, malaria, typhoid and recurrent fevers, measles, etc., etc., but only in a few of them has the absolute dependence of the disease on the presence of the bacterium been demonstrated. Many difficulties lie in the way of affording this proof, chief of which are the inability to cultivate the germs outside of the body, and the insusceptibility of animals in whom they are inoculated. Thus gonorrhœal micrococci, cultivated in sterilized media through several generations, while producing a most unmistakable clap when introduced into human urethræ, prove harmless to animals.

When we review all the facts relating to the germ theory of disease, a brief outline of which we have attempted here, it seems to us that the odds are overwhelmingly in its favor; that by it conditions are explained for which there is no other satisfactory solution; and that it casts a clear light on questions which have baffled all previous investigation. It will, of course, like the theory of evolution, be combated for a number of years to come, especially by the strongly conservative members of the profession, who find it hard to throw off the traditions of years, but Time, which healeth all things, will cure this disposition too.

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